REMARKS

This communication is in response to the outstanding Official Action dated January 30, 2001, the shortened statutory period for filing a response expiring on April 30, 2001. In view of the amendments and remarks, reconsideration of the Examiner's rejection is requested and a Notice of Allowance of all pending claims is respectfully requested.

The Examiner has acknowledged Applicant's election of Group II, claim 11-28 directed to the method of administering bee venom. Additionally, Applicant selected treatment of a patent suffering from rheumatoid arthritis in response to the Examiner's requirement that Applicant select a single disclosed species for prosecution. Applicant notes that the Examiner refers to Group II claims as being claims 12-18 in the detailed action which appears to be inadvertent. Claims 1-10 and 29-30 were withdrawn from further consideration by the Examiner as being drawn to nonelected inventions. Accordingly, claims 11-28 are addressed in this Amendment and Remarks.

The specification has been objected to as failing to provide proper antecedent basis for claimed subject matter. Specifically, claim 25 recites that the anesthetic is administered in amount of about 0.1 mg to about 0.3 mg per injection. However, the specification does not have the corresponding language. Accordingly, Applicant has amended the specification at page 14 to include the amount of 0.1 mg to about 0.3 mg per injection of anesthetic in response to this objection. As the subject matter was part of the claims as originally filed, this amendment to the specification does not constitute the addition of new matter.

Claims 12-14, 16-21, 23-25 and 27 have been objected to because of various informalities. Applicant has amended the claims to address these informalities.

Turning to the substantive rejections, claims 11, 22, and 26 have been rejected under 35 U.S.C. § 102(b) as being anticipated by *Steigerwaldt et al.* *Steigerwaldt et al.* is said to teach the use of bee venom and local anesthetic for therapeutic application including rheumatoid arthritis. The bee venom and local anesthetic is said to have been given in therapeutically effective amounts to patients by intradermal injection.

Applicant respectfully traverses. A careful review of *Steigerwaldt et al.* reveals that it teaches intradermal injection of a form of bee venom in isotonic solution. The reference notes that procaine hydrochloride 0.2% is used as a local anesthetic. *Steigerwaldt et al.* teaches that only the bee venom is administered by intradermal injection. It neither teaches nor suggests injection rather than, for example, topical application.

Thus, *Steigerwaldt et al.* neither teaches nor suggests Applicant's invention of intradermal injection either simultaneously or consecutively of a therapeutic effective amount of bee venom intradermally and an anesthetic intradermally. Accordingly, the claims are not anticipated and the rejection should be withdrawn.

Claims 11, 22, 26 and 27 are rejected under 35 U.S.C. § 103(a) as being unpatentable over *Steigerwaldt et al.* in view of Ogram *et al.*, U.S. Patent No. 6,029,863. *Steigerwaldt et al.* is said to teach the use of bee venom and local anesthetic, such as procaine, for therapeutic use including rheumatoid arthritis. *Steigerwaldt et al.* however does not disclose the use of lidocaine as local anesthetic in the same method. *Ogram et al.* is thus relied upon as teaching the use of lidocaine as a specific local anesthetic to reduce pain resulting from bee stings thereby having a calming effect on the victim. The Examiner believes it would be obvious to one of ordinary skill in the art to substitute procaine with lidocaine since both are

known to reduce pain associated with bee stings. *Steigerwaldt et al.* does not teach Applicant's invention with the mere difference being the use of procaine versus lidocaine.

While previous methods of apitherapy involved the use of conventional topically applied anesthetics in an attempt to alleviate pain, irritation and swelling associated with apitherapy, such methods were inadequate. *Steigerwaldt et al.* is an example of such method. The inventor discovered that conventional topically applied anesthetics were ineffective in overcoming or reducing apitherapy side effects. Although they can lessen the discomfort associated with being stuck by a needle, they do little to alleviate the irritation caused by the injected bee venom.

Applicant has found, quite unexpectedly, that anesthetics, particularly topical or local anesthetics, can be injected along with the bee venom, or shortly before or after, directly into or adjacent the bee venom injection site. When applied in this manner, even in doses and concentrations far lower than those normally used for topical and local applications for treatments as painful as bee venom, such as below 2%, it has been found that the irritation associated with an injection of bee venom can be reduced appreciably. See claims 12-14 and 23-25. Indeed, while anesthetics may be used in amounts of 1 to 2% topically, much more is often required for very painful procedures. Applicant found it very surprising to learn that amounts as low as 2 mg per injection and less produce meaningful reductions in discomfort. It was particularly surprising to observe these advantages at only 10 times the amount of venom administered and below.

Not only was the amount of anesthetic used when applied in this fashion surprising, so too was the way in which it acted. Anesthetics applied topically and intradermally would be expected, at these concentrations and quantities, to provide some

form of pain relief for only a few moments. That might help with the initial pain of the injection. However, bee venom could be very painful for as much as 10 to 15 minutes after injection, much longer than such a small dose of anesthetic could be expected to provide any relief. Yet it was surprisingly found that anesthetics applied in the manner of Applicant's invention could actually provide adequate pain relief long after the injection. Indeed, pain relief was consistent. That is to say that the patients did not, after 5 to 10 minutes, suddenly realize a higher level of pain as the anesthetic wore off.

In view of the above remarks, the Patent Office has failed to establish a *prima facie* case of anticipation or obviousness based upon the applied references.

Applicant respectfully submits that all claims presently set forth in this application possess the requisite novelty, utility and nonobviousness to warrant their immediate allowance, which action is respectfully solicited.

Finally, Applicant requests the opportunity of an interview with the Examiner at the time when the Examiner is reconsidering the case.

If, however, for any reason the Examiner does not believe that such action can be taken at this time, it is respectfully requested that he telephone applicant's attorney at (908) 654-5000 in order to overcome any additional objections which he might have.

If there are any additional charges in connection with this requested amendment, the Examiner is authorized to charge Deposit Account No. 12-1095 therefor.

Respectfully submitted,

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MARKED-UP COPY OF AMENDED SPECIFICATION PARAGRAPHS:

Amend the paragraph beginning at page 14, line 25 and ending at page 14, line 28 as follows:

The amount of anesthetic administered is preferably between about 0.01 and about 2.0mg per injection and more preferably between about 0.05 and about 1.0mg per injection. Most preferably, the amount of anesthetic administered in each injection is about 0.1mg to about .03 mg per injection.

MARKED-UP COPY OF AMENDED CLAIMS:

12. The method of claim 11 wherein said anesthetic is administered in a ratio of between about 20:1 to ~~-~~1:10 by weight relative to the weight of said bee venom.

13. The method of claim 12 wherein said anesthetic is provided in a ratio of between about 10:1 to ~~-~~1:5 by weight relative to the weight of said bee venom.

14. The method of claim 13 wherein said anesthetic is provided in a ratio of about 3:1 to ~~-~~1:1 by weight relative to the weight of said bee venom.

16. The method of claim 15 wherein said at least one excipient or liquid carrier are provided in an amount which is sufficient to provide between about 0.1 mg and about 10.0 mg of bee venom per mL.

17. The method of claim 16 wherein said at least one excipient or liquid carrier are provided in an amount which is sufficient to provide about 0.5 mg and about 5.0 mg of bee venom per mL.

18. The method of claim 17 wherein said at least one excipient or liquid carrier are provided in an amount which is sufficient to provide about 1.0 mg of bee venom per mL

19. The method of claim 15 wherein said be venom is administered in an amount of between about 0.01 mg and about 1.0 mg per injection.

20. The method of claim 19 wherein said be venom is administered in an amount of between about 0.05 mg and about 0.5 mg per injection.

21. The method of claim 20 wherein said bee venom is administered in an amount of about 0.1 mg per injection.

23. The method of claim 15 wherein said anesthetic is administered in an amount of between about 0.01 mg and about 2 mg per injection.

24. The method of claim 23 wherein said anesthetic is administered in an amount of between about 0.05 mg and about 1.0 mg per injection.

25. The method of claim 24 wherein said anesthetic is administered in an amount of about 0.1 mg to about 0.3 mg per injection.

28. The method of claim 11 wherein said bee venom has the purity equivalent to that resulting from filtering through a 25 micron~~mcm~~ filter.